4. INTRODUCTION

This protocol is designed to investigate the use of a vaccination approach in the treatment of human B-cell lymphoma. Previous work has shown that active vaccination of patients with idiotype (Id) protein can induce an anti-idiotype immune response (1). Patients developing an anti-Id immune response had a remission of longer duration and a prolonged survival compared to the patients without immune response and compared to historical control patients (2). Unfortunately, the process of producing the Id proteins needed for a customized vaccine is difficult and time consuming, and adequate vaccine protein production is achieved in only about 80% of the cases. Also, the adjuvants needed for optimal effect of the vaccine often cause substantial side effects. These limitations prevent widespread use of this promising vaccine approach. Therefore, new techniques are needed to induce a tumor-specific immune response in patients.

Recently, researchers at Vical Incorporated showed that plasmid DNA injected into skeletal muscle is taken up by cells which then produce the specific protein encoded by the plasmid. Using this technique, investigators in Dr. Ronald Levy's lab at Stanford University have shown that animals vaccinated with plasmid coding for tumor specific idiotype were protected against subsequent tumor challenge. It was learned that the variable regions of the tumor immunoglobulin had to be linked to xenogeneic constant regions or to cytokine fragments to be effective (3). Constructs containing syngeneic constant regions as well as constructs containing the variable regions alone (as scFv) were not protective as DNA vaccines. No adverse effects of these immunizations were observed.

In this Phase I/II protocol, we propose to immunize low-grade non-Hodgkin's B-cell or mantle cell lymphoma patients with a plasmid coding for their specific tumor idiotype linked to murine constant regions. Patient tumor cells will be harvested and B-cell immunoglobulin variable regions isolated at Stanford University Medical Center by the study investigators and sent to Vical Inc. for production of the specific plasmids. It is known from previous therapies utilizing murine monoclonal antibodies that the possible induction of human anti-mouse antibodies (HAMA) produces no adverse effects in patients. The specific objectives of this study are to evaluate (a) the safety and toxicity of the therapy, (b) the induction of an immune response, both humoral and cellular, against the idiotype of the surface tumor immunoglobulin and (c) any anti-tumor effect.